

REMARKS/ARGUMENTS

This RCE Request is submitted so that the Examiner will consider the functional data referenced in the prior Affidavit by Mark Zoller. As attested to therein, this data (contained in Figure 2) substantiates that hT2R76 is a bitter taste receptor as correctly disclosed in the as-filed specification and specifically responds to the bitter ligands brucine and PROP. As indicated previously, PROP is among the bitter ligands disclosed in the as-filed specification that was indicated to be a ligand that potentially would specifically activate hT2R76.

Based on this functional data, the prior §112 written description and enablement rejections should be vacated.

Additionally, Applicants provide herewith a copy of a Board of Appeals Decision in US Serial No. 09/825,882 wherein the Board of Appeals and Interferences reversed a rejection of hT2R claims based on later-obtained data demonstrating that the hT2R sequence in dispute did encode a functional bitter taste receptors, i.e., a human taste receptor that specifically responds to bitter ligands.

The reasoning of the Board's reversal of the Examiner's rejections therein are directly on point to the rejections made in the present application.

Based on the foregoing, withdrawal of the prior §112 rejections is respectfully requested.

As a final note, Applicants advise that a supplemental §131 Affidavit signed by the inventors excepting Elliot Adler is to be submitted.

If the Examiner has any questions relating to this application, she is respectfully requested to contact the undersigned.

Appln. No. 10/628,464
Reply dated June 22, 2006
In Response to Final Office Action 2/22/2006

Please grant any extension of time required to enter this response and charge or credit any variance of the amount enclosed to our Deposit Account Number 50-0206.

Respectfully submitted,

HUNTON & WILLIAMS LLP

By:



Robin L. Teskin
Registration No 35,030

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Hunton & Williams LLP
Intellectual Property Department
1900 K Street, N.W.
Suite 1200
Washington, DC 20006-1109
(202) 955-1500 (telephone)
(202) 778-2201 (facsimile)

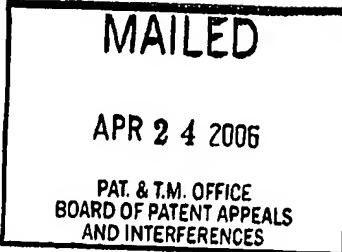
The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte JON ELLIOT ADLER

Appeal No. 2006-0157
Application No. 09/825,882



HEARD: March 23, 2006

Before SCHEINER, MILLS, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to nucleic acids encoding a bitter taste receptor. The examiner has rejected the claims as lacking utility, non-enabled, and inadequately described. We have jurisdiction under 35 U.S.C. § 134. We reverse all of the rejections.

Background

"Mammals are believed to have five basic taste modalities: sweet, bitter, sour, salty, and umami (the taste of monosodium glutamate)." Specification, page 1. "Each taste modality is believed to be mediated by distinct transduction pathways. These pathways are believed to be mediated by receptors . . . expressed in subsets of taste receptor cells." Id.

The specification discloses a "family of G Protein-Coupled Receptors . . . thought to be primarily involved in bitter taste transduction." Page 4. The family of proteins is known as the "T2R" family; the nucleic acid sequence of human T2R61 is shown in the specification's SEQ ID NO:7 and the encoded amino acid sequence is shown in SEQ ID NO:8.

The specification discloses that T2R proteins are useful for, among other things, "screening for modulators, e.g., activators, inhibitors, stimulators, enhancers, agonists, and antagonists, of these novel taste-cell-specific GPCRs. . . . These methods of screening can be used to identify high affinity agonists and antagonists of taste cell activity. These modulatory compounds can then be used in the food and pharmaceutical industries to customize taste, for example, to decrease or mask the bitter taste of food or drugs." Page 9. See also page 3: "Such taste modulating compounds could be useful in the pharmaceutical and food industries to improve the taste of a variety of consumer products, or to block undesirable tastes, e.g., bitter tastes, in certain products."

Discussion

1. Claim construction

Claims 158-185 are pending and on appeal. Claims 158 and 159 are representative and read as follows:

158. An isolated nucleic acid molecule encoding a bitter taste receptor selected from the group consisting of

(i) an isolated nucleic acid sequence having the nucleic acid sequence contained in SEQ ID NO:7;

(ii) a nucleic acid sequence that encodes the bitter taste polypeptide contained in SEQ ID NO:8;

(iii) an isolated DNA sequence that hybridizes under stringent hybridization conditions to the nucleic acid sequence contained in SEQ ID NO:7 wherein stringent hybridization conditions are hybridization in 5 x SSC, 1% SDS, incubated at 65°C and wash in 0.2 x 55C [sic, SSC] and 0.1% SDS at 65°C, wherein said hybridization and wash steps are each effected for at least 1 minute.

159. An isolated nucleic acid molecule encoding a bitter taste receptor polypeptide which polypeptide comprises at least 95% identity to the taste receptor polypeptide contained in SEQ ID NO:8.

Thus, claim 158 is directed to SEQ ID NO:7, another nucleic acid that encodes the amino acid sequence of SEQ ID NO:8, or a DNA sequence that hybridizes under specified, stringent conditions to SEQ ID NO:7. Claim 159 is directed to a nucleic acid that encodes a polypeptide that is at least 95% identical to SEQ ID NO:7. Both claims also require that the nucleic acids encode functional bitter taste receptors.¹

2. Utility

The examiner rejected claims 158-185 under 35 U.S.C. §§ 101 and 112, first paragraph, on the basis that the specification does not disclose a patentable utility for the claimed nucleic acids. The examiner reasoned that

[t]he concept of "bitter taste" is known to involve multiple and as yet poorly characterized transduction schemes. . . . These transduction schemes are also thought to involve a large diversity of receptors. . . . The specification has given no indication as to which of these [bitter-tasting] compounds is expected to bind to and activate SEQ ID NO:8. Without such knowledge, the artisan could not use the protein to manipulate any aspect of the senses involving taste.

¹ The version of claim 159 in the appendix to the Appeal Brief includes the final clause ", wherein sequence identity is determined by any one of the BLAST, BLAST 2.0 or PILE UP algorithms." This clause does not appear in the claim added by amendment on May 14, 2004. Appellant should check the claims in the official Image File Wrapper to ensure that they read as desired. The examiner should check the claims to ensure that they include all necessary limitations.

Examiner's Answer, pages 4-5. The examiner acknowledged that the "specification puts forth that the polypeptides are useful for 'representing the perception of taste and/or for predicting the perception of taste in a mammal,' " "as probes to dissect taste-induced behaviors," and "in a screening method to determine what molecules may activate or inhibit the polypeptides," but concluded that "[t]hese proposed uses lack a substantial utility, because each of the proposed uses [is] of a general nature." Id., page 5.

Appellant argues that the evidence of record supports the specification's assertion that SEQ ID NO:8 is a bitter taste receptor. See the Appeal Brief, pages 11-15. Appellant also argues that "most significantly, and as correctly disclosed in the as-filed application, the subject T2R nucleic acid sequences, based on their reasonably anticipated . . . functionality as bitter taste receptors can be used in high throughput screens to identify compounds which modulate the activity of this receptor." Id., page 20.

The U.S. Court of Appeals for the Federal Circuit recently addressed the utility requirement as applied to a claim to DNA. See In re Fisher, 421 F.3d 1365, 1371, 76 USPQ2d 1225, 1229 (Fed. Cir. 2005). The Fisher court held that § 101 requires a utility that is both substantial and specific. Id. at 1371, 76 USPQ2d at 1229. A substantial utility is one that "show[s] that an invention is useful to the public as disclosed in its current form, not that it may be useful at some future date after further research. Simply put, to satisfy the 'substantial' utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public." Id., 76 USPQ2d at 1230.

A specific utility is one " which is not so vague as to be meaningless." Id. In other words, "in addition to providing a 'substantial' utility, an asserted use must show that that claimed invention can be used to provide a well-defined and particular benefit to the public." Id.

When we apply the standards set out in Fisher to the facts of this case, we conclude that the examiner's rejection must be reversed. As we understand it, the examiner does not dispute that the protein encoded by the claimed nucleic acids is a bitter taste receptor, but contends that those skilled in the art could not use the protein in any specific and substantial way without first knowing what compounds were bound by it.

We find this position untenable. The specification discloses that the hT2R61 protein can be used in screening assays to identify compounds that bind the protein. Given the undisputed characterization of the protein as a bitter taste receptor, it seems reasonable to expect that some of those compounds would be antagonists that would block the perception of bitter taste by the receptor. As Chandrashekhar² put it, "the identification of human bitter taste receptors makes it possible to use high-throughput screening strategies to identify bitter taste antagonists, and in a small but significant way, eliminate bitterness from the world." Page 710.

This utility is disclosed in the specification (see page 9) and relied on in the Appeal Brief (see page 20). It also seems to us to be a "substantial" and "specific" utility, as defined by the Fisher court: identifying compounds that can block the bitter

² Chandrashekhar et al., "T2Rs function as bitter taste receptors," Cell, Vol. 100, pp. 703-711 (2000). Chandrashekhar was incorporated by reference into the specification. See page 8, lines 14-15.

taste of foods or medicines would seem to provide a significant, presently available, and well-defined benefit to the public.

The examiner bears the initial burden of showing that a claimed invention lacks patentable utility. See In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995). In this case, however, the examiner's explanation of the rejection (Examiner's Answer, pages 4-8) does not address this asserted utility. The examiner's reasoning does not persuade us that the disclosed utility is inadequate to meet the requirements of 35 U.S.C. § 101. We therefore reverse the rejections under 35 U.S.C. §§ 101 and 112, first paragraph, based on lack of utility.

3. Scope of enablement

The examiner also rejected claims 158, 159, and 164-185 under 35 U.S.C. § 112, first paragraph, on the basis that "the specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims." Examiner's Answer, page 8. The examiner noted that these claims "encompass polynucleotides encoding polypeptide variants of the polypeptide of SEQ ID NO:8[.] i.e., substitutions, deletions or insertions." Id., pages 8-9. The examiner reasoned that "the specification has failed to teach one of ordinary skill in the art which amino acid substitutions, deletions or insertions to make that will preserve the structure and function of the protein," that "no particular ligand has been disclosed to bind and activate the protein, so the artisan would not know how to test variants for functionality," that the specification provides no working examples of hT2R61 variants, and that the prior art (including Chandrashekhar) "recognizes the complexity, unpredictability, and non-routine nature of the work involved in trying to assay functional T2R receptors." Id.,

pages 9-11. The examiner concluded that undue experimentation would be required to make and use the claimed variants.

Appellant argues that the claimed genera are limited to nucleic acids with a high degree of similarity to SEQ ID NO:7 or encoding a protein very similar to SEQ ID NO:8, that such variants can be made or isolated routinely, and that the specification "provides substantial information relating to T2R assays that would enable one skilled in the art to screen these variant hT2R61 nucleic acid sequences and identif[y] those variants that are functional, i.e., bind the same bitter ligands which specifically interact with wild-type hT2R61 polypeptide." Appeal Brief, pages 25-27.

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). "That some experimentation may be required is not fatal; the issue is whether the amount of experimentation required is 'undue.'" In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). Whether the amount of experimentation required is undue is determined by reference to the well-known Wands factors. See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In this case, we agree with Appellant that the examiner has not shown, by a preponderance of the evidence, that practicing the full scope of the claims would have required undue experimentation. The examiner's position rests in part on the lack of guidance in the specification regarding amino acids in hT2R61 that can be altered or deleted without affecting its function.

It is true that the specification does not teach which specific amino acids are critical to hT2R61 function. However, the specification does provide substantial guidance to those skilled in the art. The specification provides the nucleotide and amino acid sequences shown in SEQ ID Nos 7 and 8, which correspond to human T2R61. The specification (page 8, lines 13-15) also incorporates by reference the sequence comparison disclosed by Adler.³ Adler provides a sequence comparison of twenty-three human, mouse, and rat T2R amino acid sequences. The comparison does not include human T2R61 but the examiner has given us no reason to think that the same techniques used by Adler could not be applied by a person skilled in the art to the T2R61 sequence of the instant specification.

Adler's sequence comparison identifies each of the seven transmembrane (TM) domains, and shows conserved regions between TM1 and TM2, between TM3 and TM4, and between TM5 and TM6. By comparison, the regions between TM2 and TM3, between TM4 and TM5, and between TM6 and TM7 are much less conserved. Such sequence comparisons provide guidance to those skilled in the art regarding which regions of the T2R proteins are likely to be required for function: changes in conserved regions are more likely to disrupt function of the protein than changes in non-conserved regions. Thus, Adler guides a skilled worker to areas of hT2R61 that are likely to be tolerant of amino acid changes.

The specification also discloses assays for determining whether hT2R61 variants retain the activity of the wild-type protein. See pages 50-65 (discussing numerous assays to test for binding of a T2R receptor to putative taste modifiers). Chandrashekhar

³ Adler et al., "A novel family of mammalian taste receptors," Cell, Vol. 100, pp. 693-702 (2000).

provides evidence that such assays identify functional bitter taste receptors. See the abstract: "[W]e use a heterologous expression system to show that specific T2Rs function as bitter taste receptors. A mouse T2R (mT2R-5) responds to the bitter tastant cycloheximide, and a human and a mouse receptor (hT2R-4 and mT2R-8) responded to denatonium and 6-n-propyl-2-thiouracil."

Finally, Appellant has presented post-filing evidence, which the examiner has considered (Examiner's Answer, page 17), confirming that the methods disclosed in the specification demonstrate that hT2R61 interacts with several compounds that elicit a bitter taste. See the evidence attached to the Appeal Brief as Exhibit 3.

On the facts of this case, we must agree with Appellant that the examiner has not adequately explained why practicing the full scope of the claims would have required undue experimentation. The prior art, which was incorporated by reference into the specification, provides substantial guidance with respect to the direction the experimentation should proceed. The process of making and assaying hT2R61 variants would appear to be routine, if tedious, experimentation. The claims are limited to variants having 5% or less variation compared to SEQ ID NO:8 and those hybridizing to SEQ ID NO:7 under stringent conditions. In view of these factors, we cannot say that the examiner has shown nonenablement by a preponderance of the evidence. The rejection of claims 158, 159, and 164-185 for lack of enablement is reversed.

4. Written description

The examiner also rejected claims 158, 159, and 164-185 under 35 U.S.C. § 112, first paragraph, on the basis that "the claims encompass polynucleotides not described in the specification, e.g., mutated sequences, allelic variants, or sequences

that have a recited degree of identity. None of these sequences meet the written description provision of 35 U.S.C. § 112, first paragraph." Examiner's Answer, page 12.

The examiner reasoned that

[t]he specification has not provided a particular essential feature, either a functional or structural feature, that the claimed genus of polynucleotides possess[es]. The recitation of the property of hybridization does not, alone, provide sufficient information regarding the structure of the claimed polynucleotide variants. Further, most of these variants are expected to encode polypeptides having an amino acid sequence different than that of SEQ ID NO:8 and thus having different structural and functional properties.

Id., page 13.

The examiner "bears the initial burden . . . of presenting a prima facie case of unpatentability.' In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Insofar as the written description requirement is concerned, that burden is discharged by 'presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims.'" In re Alton, 76 F.3d 1168, 1175, 37 USPQ2d 1578, 1583 (Fed. Cir. 1996).

Several recent Federal Circuit decisions have addressed the written description of inventions involving DNA. In University of California v. Eli Lilly and Co., the court held that "[a]n adequate written description of a DNA . . . 'requires a precise definition, such as by structure, formula, chemical name, or physical properties.'" 119 F.3d 1559, 1566, 43 USPQ2d 1398, 1404 (Fed. Cir. 1997). The Lilly court noted that, when a genus of compounds is claimed, those skilled in the art can "visualize or recognize the identity of the members of [a fully described] genus" and held that "[a] description of a genus of DNAs may be achieved by means of a recitation of a representative number of DNAs,

defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id. at 1568, 43 USPQ2d at 1406.

The court clarified the Eli Lilly standard in Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" Id. at 964, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

Finally, the court has made clear that other factors, including the level of skill in the art, are relevant to whether a description satisfies § 112. See Capon v. Eshhar, 418 F.3d 1349, 1358-59, 76 USPQ2d 1078, 1085 (Fed. Cir. 2005) ("Precedent illustrates that the determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter.").

When we apply the appropriate legal standard to the facts of this case, we conclude that the examiner's rejection must be reversed. The claims are limited to nucleic acids that hybridize under stringent conditions to SEQ ID NO:7 or that encode polypeptides at least 95% identical to SEQ ID NO:8. Thus, the claimed nucleic acids

will necessarily have a high degree of structural similarity to SEQ ID NO:7; in other words, each of the claimed nucleic acids shares something like 95% of its structure with SEQ ID NO:7.

Although the specification's disclosure does not allow those skilled in the art to know, without testing, which of the hybridizing or 95% similar sequences will encode a polypeptide that shares hT2R61's bitter taste receptor function, the specification teaches numerous assays that can be used to make that determination. See pages 50-65. The prior art Chandrashekhar reference provides evidence that carrying out such assays was within the level of ordinary skill. See pages 703-707.

Because the claimed nucleic acids are very similar in structure to SEQ ID NO:7 and because assays that are disclosed in the specification and apparently routine to those skilled in the art can be used to distinguish between functional and nonfunctional embodiments, we conclude that a person of ordinary skill in the art would have recognized from the specification's description that the inventors were in possession of the claimed nucleic acids. The rejection of claims 158, 159, and 164-185 for lack of adequate written description is reversed.

Other Issue

We note that the scope of claim 158 includes "(ii) a nucleic acid sequence that encodes the bitter taste polypeptide contained in SEQ ID NO:8." The claim as written does not require the nucleic acid encoding SEQ ID NO:8 to be isolated or purified, and therefore may read on a nucleic acid (e.g., mRNA or genomic DNA) as it exists naturally. We encourage the examiner and Appellant to review the claim and work together to resolve any lingering problems with claim language.

Summary

We conclude that the evidence of record does not support the rejections for lack of utility, nonenablement, and lack of adequate written description. The rejections on appeal are reversed.

REVERSED



TONI R. SCHEINER)
Administrative Patent Judge)

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Demetra J. Mills)
DEMETRA J. MILLS)
Administrative Patent Judge)

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Eric Grimes)
ERIC GRIMES)
Administrative Patent Judge)

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) APPEALS AND
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) INTERFERENCES
)

EG/lbg

DUANE MORRIS LLP
SUITE 700
1667 K STREET
WASHINGTON, DC 20006